Burden of Disease and Treatment Patterns Amongst Patients With Vitiligo: Findings From a National, Longitudinal Retrospective Study in the United Kingdom

Running Head: Vitiligo: UK Burden and Treatment Patterns

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Data availability: Access to individual participant-level data is not publicly available for this study.

Ethics statement: The study protocol was approved by the CPRD Research Data Governance process (protocol reference: 22_001820).

What is already known about this topic?

- Prevalence of diagnosed vitiligo is estimated between 0.2%–0.8% in Europe with geographic and methodologic differences
- The burden of disease is considerable, and vitiligo can have a profound impact on an individual's psychosocial well-being and quality of life
- Patients with vitiligo are often affected by other autoimmune disorders and mental health conditions
- Studies examining the burden of vitiligo on patients and the healthcare system in the United Kingdom are lacking

What does this study add?

- From UK Clinical Practice Research Datalink and Hospital Episode Statistics databases, vitiligo incidence was 0.16/1000 person-years; 2021 prevalence was 0.38%
- In 2019, 85.0% of prevalent patients had no record of vitiligo-related treatment
- Median time before first vitiligo-related treatment was 34 months (incident cohort) after diagnosis; most commonly topical and oral corticosteroids, topical calcineurin inhibitors
- The year after diagnosis, 16.7% of incident patients had treatment with antidepressants and/or anxiolytics recorded

Abstract

This retrospective study, using UK Clinical Practice Research Datalink and Hospital Episode Statistics databases, analysed 17,239 incident patients with vitiligo. Mean incidence of vitiligo was 0.16 (2010–2021) per 1000 person-years (range: 0.10 [2010-COVID] to 0.19 [2013/2018]); prevalence increased from 0.21% (2010) to 0.38% (2021). The most common comorbidities recorded after vitiligo diagnosis were diabetes (19.4%), eczema (8.9%), thyroid disease (7.5%), and rheumatoid arthritis (6.9%). Mental health diagnoses recorded at any time were most commonly depression and/or anxiety (24.6%), depression (18.5%), anxiety (16.0%), and sleep disturbance (12.7%); recorded after vitiligo diagnosis in 6.4%, 4.4%, 5.5%, and 3.9%, respectively. Mental health comorbidities were more common among White patients (eg, depression and/or anxiety, 29.0%) than Black (18.8%), Asian (16.1%), and other ethnicities (21.4%). In adolescents, depression and/or anxiety was most commonly diagnosed after vitiligo diagnosis (7.4% vs before, 1.8%).

Healthcare resources were used most frequently in the first year after vitiligo diagnosis (incident cohort), typically dermatology-related outpatient appointments (101.9/100 person-years) and general practitioner consultations (97.9/100 person-years). In the year after

diagnosis, 60.8% of incident patients did not receive vitiligo-related treatments (ie, topical corticosteroids, topical calcineurin inhibitors, oral corticosteroids, phototherapy), increasing to 82.0% the next year; median (95% CI) time from diagnosis to first treatment was 34.0 (31.6–36.4) months. Antidepressants and/or anxiolytics were recorded for 16.7% of incident patients in the year after diagnosis. In 2019, 85.0% of prevalent patients did not receive vitiligo-related treatments; 16.6% had a record of antidepressant and/or anxiolytic treatments.

Most patients were not on vitiligo-related treatments within a year of diagnosis, with time to first treatment >2 years, suggesting that vitiligo may be dismissed as unimportant and not treated early, in part due to limited effectiveness of available treatments. New effective treatments, early initiation, and psychological intervention and support are needed to reduce vitiligo burden on patients.

Introduction

Vitiligo is a chronic autoimmune disease characterised by selective loss of melanocytes, resulting in patches of skin depigmentation.[1,2] Data regarding vitiligo incidence are scarce; the European diagnosed prevalence of vitiligo ranges from 0.2%–0.8%, with geographic and methodologic differences.[1,3,4]

Vitiligo can have a profound impact on the psychosocial well-being and quality of life for patients.[5-9] Furthermore, comorbid autoimmune disorders and mental health diagnoses can further affect well-being and quality of life.[5-9] The prevalence of vitiligo comorbidities in the United Kingdom (UK) has not been investigated.

In chronic disease, increased healthcare resource utilisation (HCRU) is associated with financial loss (eg, disease-related lost work hours) contributing to disease burden. Data captured in databases such as the Clinical Practice Research Datalink (CPRD) Aurum and Hospital Episode Statistics (HES) databases include patient demographics, medical diagnoses,

drug exposure, procedures, laboratory and pathology test results, hospital and specialist referrals, details of admissions, emergency attendances, and outpatient appointments at National Health Service (NHS) hospitals in England. Together, these data can be used to assess disease burden and disease-associated HCRU.

UK studies examining vitiligo burden and vitiligo-related HCRU are lacking. This longitudinal retrospective descriptive study, using large national UK clinical databases, describes the incidence and prevalence of vitiligo, demographic and clinical characteristics of patients with vitiligo, and vitiligo burden. HCRU, incidence of mental health comorbidities, and management strategies including treatment patterns are described.

Methods

Study Design and Patients

This retrospective study used data from the CPRD database that was linked to the HES database. CPRD Aurum contains data collected since 1995 and covers ~40 million patients (historic and current), including ~13 million patients currently registered with a general practitioner (GP).

The incident cohort included patients with a vitiligo diagnosis in the CPRD database who were aged ≥12 years at the time of first vitiligo diagnosis, and the prevalence cohort included those aged ≥12 years during the study period. Exclusion criteria included diagnosis of vitiligo due to pinta or as part of a congenital disorder, vitiligo of the iridis, or occupational vitiligo. The overall study period was from January 1, 2010, until December 31, 2021.

Objectives

Primary objectives were to (1) determine the annual incidence and prevalence of vitiligo for each year from 2010 to 2021; (2) describe demographic and clinical characteristics of patients first diagnosed with vitiligo from 2010 to 2019, including comorbidities; and (3) describe treatment patterns, including time from diagnosis to treatment initiation and HCRU from 2010 to 2019 for UK patients with vitiligo.

Endpoints and Analyses

Incidence and prevalence cohorts

Annual incidence and prevalence rates were calculated for 2010 through 2021, with incidence being the rate of incident vitiligo diagnoses within each calendar year, and prevalence calculated as the point prevalence on January 1 of each year; additional criteria follow. For the incident cohort, the index date was the date of vitiligo diagnosis; patients were followed until the earliest of practice registration end date, last practice collection date, end of study period for the specific endpoint, or patient death. Patients lost to follow-up were censored from the date of loss onward. Annual incidence for each calendar year was calculated as the number of patients ≥12 years old with a new diagnosis of vitiligo in that calendar year divided by the person-time at risk (ie, total period within the year that patients were ≥12 years) within that year and reported as incidence per 1000 person-years. The point prevalence of vitiligo was calculated on January 1 of each year (2010–2021) as all patients ≥12 years with a pre-existing vitiligo diagnosis on or before January 1 and still registered with a contributing GP at that time divided by the total number of patients registered with a contributing GP on that date.

Demographics and clinical characteristics

Demographic and clinical characteristics at the time of vitiligo diagnosis were described for incident cases only, as were comorbidities in the 5 years before and after diagnosis. The patient journey and disease burden were assessed by HCRU (reported per 100 person-years), the incidence of mental health comorbidities, and the time from diagnosis until initiation of vitiligo-related treatment.

HCRU

HCRU was assessed as vitiligo-related primary care consultations (in-person and telephonic) with GPs, nurses, and other healthcare professionals and dermatology-related hospital events (ie, inpatient admissions, outpatient visits, accident and emergency visits). Treatment patterns were identified using prescription or treatment records, which were used to estimate the time between initial diagnosis and start of the first, second, and third vitiligo-related treatments.

Treatment patterns

Prescription or treatment records of interest were categorised as vitiligo-related treatments (ie, topical calcineurin inhibitors, topical corticosteroids, oral corticosteroids, light therapies, which included narrowband ultraviolet B [NB-UVB] phototherapy and psoralen ultraviolet A photochemotherapy, and laser therapies), and non–vitiligo-related treatments (ie, all other treatment records other than vitiligo-related), adjuvant management strategies (ie, sunscreen, vitamin D, camouflage prescription, referral to camouflage services, and referral to dermatologists), and psychological management strategies (ie, antidepressants, anxiolytics, and psychological intervention referrals). For reporting of HCRU and treatment usage by calendar year, prevalent patients were those with follow-up data available in that particular year. The

analysis of treatment patterns over time (ie, Sankey analysis) included incident patients who were included in the HES outpatient database, a database containing records of light therapy, and diagnosed no later than December 31, 2018, to allow for a potential 1-year minimum follow-up period. Treatment events (defined as a change in treatment) were identified up to the fourth event. At the end of follow-up, if patients did not have 4 treatment events, their final event was recorded as "no further treatment, <18 months since last treatment" or "no further treatment, ≥18 months since last treatment record." A period of 18 months without any treatment record was recorded as a "treatment gap." All analyses were descriptive.

Ethical Approval Statement

The study was performed in accordance with the Declaration of Helsinki and in adherence to the study protocol and local regulatory requirements. The study protocol was approved by the CPRD Research Data Governance process (protocol reference: 22_001820).

Results

Patients and Disposition

A total of 104,001 patients with vitiligo were identified in the CPRD database between January 1, 1995, and December 31, 2021. After excluding patients with missing or inconsistent data, those with a first vitiligo diagnosis before January 1, 2010, and those aged <12 years at diagnosis, the incident cohort included 17,239 patients with a recorded first vitiligo diagnosis between January 1, 2010, and December 31, 2019 (**Figure S1A**). The prevalent cohort included 66,217 patients with a recorded pre-existing vitiligo diagnosis on January 1 of any year between 2010 and 2021 in patients aged ≥12 years (**Figure S1B**).

Among the 17,239 incident patients, 52.2% were female (**Table 1**). Median age of patients was 41.9 (range, 12–99) years; 9.4% were adolescents (ie, 12–17 years); 65.6% were White, followed by Asian (21.2%) and Black (7.0%). At the time of vitiligo diagnosis, among those with data available, 62.5% of the incident cohort were obese or overweight, and 29.5% were current smokers.

Incidence and Prevalence

Incidence of vitiligo remained relatively stable at ~0.2 (range, 0.16–0.19) per 1000 person-years between 2010 and 2019 (**Figure 1A**). During 2020 (the first year of the COVID pandemic), the annual incidence decreased to 0.10 per 1000 person-years. The prevalence of vitiligo showed a gradual increase between 2010 and 2021, rising from 0.21% in 2010 to 0.38% in 2021 (**Figure 1B**).

Comorbidities

In the 5 years after vitiligo diagnosis, the most common comorbidities recorded among the 17,239 incident patients were diabetes (19.4%), eczema (8.9%), thyroid disease (7.5%), and rheumatoid arthritis (6.9%; **Figure 2**).

The most common mental health comorbidities in the incident cohort recorded at any time were depression (18.5%) and anxiety (16.0%), with depression and/or anxiety recorded for 24.6% of patients (**Figure S2**), including new cases recorded after vitiligo diagnosis in 4.4%, 5.5%, and 6.4%, respectively. Sleep disturbance and suicidal risk (including attempts, thoughts, risk score, or self-harm) at any time were reported in 12.7% and 7.1% of patients, respectively, including new cases recorded after vitiligo diagnosis in 3.9% and 3.2%. Mental health comorbidities were more common amongst White patients than their counterparts (**Figure S2B**).

For example, depression and/or anxiety at any time was diagnosed in 29.0% of White patients versus 18.8% of Black, 16.1% of Asian, and 21.4% of other ethnicities. Mental health comorbidities were recorded more commonly in female (30.2%) than male patients (18.5%). In contrast to findings in adults, depression and/or anxiety mostly occurred after vitiligo diagnosis in adolescents (7.4% vs before, 1.8%; **Figure S2C**).

HCRU

In the first year after vitiligo diagnosis, the rates of outpatient appointments (101.9/100 person-years) and GP appointments (97.9/100 person-years) were the highest for any of the 5 years after diagnosis (**Figure S3A**). In the fifth year, outpatient appointments and GP consultations per 100 person-years declined to 51.6 and 3.0, respectively.

In 2010, among prevalent patients with follow-up data in the specific year being analysed, dermatology-related hospital events were the most frequently used healthcare resource (8497 events; 39.8/100 person-years), most of which were outpatient appointments (8299 events; 38.9/100 person-years), with the remainder being inpatient admissions (151 events; 0.7/100 person-years) and accident and emergency visits (47 events; 0.2/100 person-years). In 2010, the rate of vitiligo-related primary care consultations was 12.7 per 100 person-years (2717 events), most of which were face-to-face GP appointments (2356 events; 11.0/100 person-years; 86.7% of vitiligo-related primary care consultations), the remainder being appointments with other healthcare professionals (361 events; 1.7/100 person-years). In 2019, the rates of dermatology-related hospital events and vitiligo-related primary care consultations per 100 person-years were 43.2 and 6.5, respectively (**Figure S3B**).

Management Strategy Patterns

In the first year after diagnosis, 60.8% of the 16,741 incident patients with data linked to the HES outpatient database had no record of any vitiligo-related treatments, which increased to ≥82.0% from the second year onward (**Figure 3A**). Of the HES-linked incident patients, in the first year, patients were recorded as having been prescribed topical corticosteroids (29.1%), topical calcineurin inhibitors (11.8%), and oral corticosteroids (4.2%). From the second year onward, the percentage of patients prescribed oral corticosteroids remained stable, while prescription of topical corticosteroids and calcineurin inhibitors declined to 11.4% and 3.9% in the second year, respectively, remaining low thereafter. In the first year after vitiligo diagnosis, 16.7% of patients were prescribed antidepressants and/or anxiolytics; prescription rates remained relatively stable across each of the 5 years following diagnosis.

Among prevalent patients with follow-up data in 2010, 66.2% of patients had no record of any treatments, and 84.3% were not receiving any vitiligo-related treatments; topical corticosteroids were prescribed for 11.1%, oral corticosteroids for 3.6%, and topical calcineurin inhibitors for 1.9% (**Figure 3B**). In 2010, the most frequently recorded adjuvant management strategies were vitamin D (5.7%), dermatology referrals (3.8%), and camouflage prescriptions (2.2%); antidepressants and/or anxiolytics, antidepressants, and anxiolytics were prescribed for 14.4%, 11.8%, and 4.4% of patients, respectively; 0.9% had record of a psychological referral. In 2019, 65.1% of prevalent patients with follow-up data had no record of any treatments either vitiligo-related or otherwise, and 85.0% were not prescribed any vitiligo-related treatments; topical corticosteroids were prescribed for 9.8% of patients, oral corticosteroids for 4.2%, and topical calcineurin inhibitors for 2.4%. In the same year, the most frequently recorded adjuvant management strategies were vitamin D (8.9%), dermatology referrals (4.0%), and camouflage prescriptions (1.2%); antidepressants and/or anxiolytics, antidepressants, and anxiolytics were

prescribed for 16.6%, 14.6%, and 4.1% of patients, respectively; 0.9% had record of a psychological referral.

Time to First Treatment

In the incident cohort, 8679 (51.8%) had ≥1 vitiligo-related treatment record during follow-up. Median duration (95% CI) from diagnosis to the first record of vitiligo-related treatment was 34.0 (31.6–36.4) months. After 1 year, 40.1% had a first vitiligo-related treatment record. Of the 8679 patients with a first vitiligo-related treatment record, 2990 (34.5%) had a second vitiligo-related treatment record; 1265 of these patients (42.3%) had a third vitiligo-related treatment record. Median time (95% CI) from diagnosis to the second and third vitiligo-related treatment was 84.4 (80.5–89.3) and 88.5 (82.5–93.7) months, respectively.

Gaps in Treatment

Overall, of the 15,105 HES-linked incident patients diagnosed before December 31, 2018, 8081 had ≥1 prescription or treatment record. Of those 8081 patients, 6549 (81.0%) had no further treatment or a treatment gap of ≥18 months (**Figure S4**). Of the 5313 patients (65.7%) who were first prescribed topical corticosteroids, 1008 (19.0%) had a recorded treatment gap following their first treatment. Among patients who had ≥2 treatment events, no clear treatment trends were identified, with small numbers of patients switching from any given treatment to another.

Discussion

Published data on the incidence of vitiligo are lacking; therefore, its determination here is a meaningful contribution to describing the epidemiology of vitiligo in the UK. The prevalence of

diagnosed vitiligo in the UK reported here falls within European estimates observed in surveys or medical screenings and is comparable to recent UK estimates (approximately 0.3%) representing the prevalence of diagnosed vitiligo in patients registered with a GP.[3,4,10] As not all patients with vitiligo seek medical attention or treatment, the actual prevalence in the UK population may be higher than observed in this dataset.[4]

Generally, the characteristics of patients with vitiligo in this study are comparable with those of the general UK population, including the percentage of patients who were overweight or obese.[11] However, the percentage of UK patients with vitiligo who were Black, Asian, or mixed or other ethnicity was higher than that among the underlying UK population.[12] This aligns with previous reports that the prevalence of vitiligo is higher in patients with darker skin,[13] which could be because those with darker skin experience a greater burden of disease[14] and therefore are more likely to seek medical care. Current smoking status in our study (29.5%) was higher than that of the general UK population (13.3%).[15] Smoking has previously been associated with other inflammatory skin disorders[16]; however, the high rate of missing data for smoking hinders definitive conclusions.

The presence of systemic and autoimmune comorbidities, as previously reported,[8] reinforces the autoimmune nature of vitiligo. Comorbidities among patients with vitiligo in our study were most often higher than those reported in individuals without vitiligo from other studies (**Figure 4**).[4,8,10,17-20] Mental health comorbidity rates were higher than rates observed in the general population (10% pre–COVID-19), including higher than post–COVID-19 rates (21%).[21] Although the presence of mental health comorbidities cannot be attributed directly to vitiligo, these comorbidities add to the disease burden associated with vitiligo. Rates of reported mental health comorbidities varied by race, sex, and age group (ie, adolescents vs adults). In contrast to the results of this study, surveys of the general population have found mental health diagnoses more infrequently among White people than people of other ethnicities.[22] It is possible that inequalities in and barriers to access to mental health services, as well as cultural

stigma associated with mental health diagnosis amongst Black and minority ethnic populations in the UK, as observed with vitiligo,[23] have led to underrepresentation of mental health diagnoses within these populations in our dataset. Nonetheless, the variance in mental health comorbidities across different demographic subgroups highlights the importance of tailored treatment approaches for vitiligo, including psychological assessment and intervention. Furthermore, to our knowledge, this study was unique in including adolescents, allowing an improved understanding of the vitiligo burden for this age group in the UK.

This study showed that in 2019 the majority of prevalent patients (85%) were not prescribed any vitiligo-related treatments. The results are consistent with previously reported surveys amongst patients with vitiligo, which found that for the majority of respondents, the priority was to find new effective treatments for lasting repigmentation, and that patients resorted to nonmedical sources (ie, internet and support groups) to obtain information about vitiligo.[14,24] Further, our results reinforce the need for early intervention.[25] We found that the majority of patients were not prescribed any vitiligo-related treatment within a year of diagnosis and that there was a median delay of ~3 years between diagnosis and first vitiligo-related treatment, which means that for patients who do receive treatment, that treatment is delayed. This is in contrast with updated British Association of Dermatology guidelines for the management of people with vitiligo, which recommend early intervention.[25] Despite the fact that patients with vitiligo may not receive any vitiligo-related treatment, they may be prescribed antidepressants and anxiolytics (16.7% in the incident cohort) within the first year of the diagnosis. Future studies investigating age-related differences in treatment uptake could enhance understanding of patient behaviour and improve healthcare strategies across age groups.

Study limitations include that the data used to assess HCRU and treatment patterns did not contain information related to prescription fulfilment, over-the-counter treatments, or private dermatologist appointments and prescriptions. Although this study lacks a control group, **Figure 4** contains data from similar studies that investigated comorbidities in individuals with and

without vitiligo. Additionally, treatment records prescribed by hospital-based dermatologists were only available if the treatment was continued by a GP. Furthermore, limited capture of phototherapy procedures in the CPRD Aurum and HES outpatient databases may have resulted in an underestimation of phototherapy utilization (treatment and frequency). These limitations could restrict the generalisability of the data. Finally, the databases used did not include vitiligo-specific measurements to assess extent of vitiligo or information on patient-reported outcomes and quality of life such as the Vitiligo-Specific Quality-of-Life instrument (VitiQoL), patients aged <12 years were not included, there was no control group, and diagnoses of vitiligo may have been made by GPs rather than dermatologists.[26]

Conclusion

This is the first broad-based UK study to estimate the incidence and prevalence of vitiligo and mental health comorbidities in patients with vitiligo. Our study showed that there is a delay in medical treatment initiation and a low specialist referral rate, which suggests that patients with vitiligo receive suboptimal care compared with recent guidelines.[25] In addition to the fact that treatments for vitiligo have variable success, lack of effective treatment contributes to the high vitiligo burden for patients. Our study highlights that new effective treatments and early treatment initiation in combination with psychological intervention are needed to reduce disease burden among UK patients with vitiligo.

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Figure Legends

Figure 1. (A) Incidence and (B) Prevalence of Vitiligo

CI, confidence interval.

Figure 2. Comorbidities in the Incident Cohort Following Vitiligo Diagnosis

AMD, age-related macular degeneration * Other dermatological comorbidities included alopecia areata and lichen planus. † Other comorbidities included myasthenia gravis, pernicious anaemia, systemic lupus erythematosus, Guillain-Barre syndrome, Sjogren syndrome, and Addison's disease.

Figure 3. Vitiligo-Related Treatment/Management Strategy Use in (A) the 5 Years After Vitiligo Diagnosis in the Incident Cohort and (B) Calendar Years 2010 and 2019 in Prevalent Patients*

* Among patients with follow-up in the relevant year. † No vitiligo-related or non–vitiligo-related treatments or management strategies. ‡ Non–vitiligo-related treatment/management strategies included psychological management strategies (ie, antidepressants and/or anxiolytics and psychological referrals) and adjuvant management strategies (ie, camouflage prescription, sunscreen, vitamin D, camouflage referrals, and dermatology referrals). § Vitiligo-related treatments/management strategies included topical corticosteroids, topical calcineurin inhibitors, oral corticosteroids, and light and laser therapy.
Red box and associated numbers denote percentage of patients not on any vitiligo-related treatments.

Figure 4. Comorbidities in the Incident Cohort and Other Study Populations

* Time window for assessing comorbidities may vary between studies. † Comparator studies investigating similar comorbidities in patients with vitiligo were found via PubMed, searching publicly available reports including relevant key words for each comorbidity paired with "vitiligo comorbidities"; our study did not distinguish between type 1 and type 2 diabetes; for comparator studies we did not include those studies reporting type 1 diabetes only. ‡ Hypothyroidism only.

Table 1. Patient Demographics and Clinical Characteristics for Incident Cohort

Characteristic	Incident Cohort (N=17,239)
Age, median (range), y	41.9 (12–99)
Adults (≥18 y), n (%)	15,623 (90.6)
Adolescents (12–17 y), n (%)	1616 (9.4)
Female, n (%)	8992 (52.2)
Race, n (%)*†	
White	10,967 (65.6)
Black	1165 (7.0)
Asian	3542 (21.2)
Other	1053 (6.3)
BMI category, n (%)*‡	
Underweight	182 (3.1)
Healthy weight	2018 (34.4)
Overweight	2047 (34.9)
Obese	1617 (27.6)
Smoking status, n (%)*§	
Non-smoker	2541 (33.5)
Ex-smoker	2805 (37.0)
Current smoker	2242 (29.5)

BMI, body mass index.
* Percentages based on those with available data.
† Data on race were not available for 512 patients.
‡ Data on BMI were not available for 11,375 patients.
§ Data on smoking status were not available for 9651 patients.

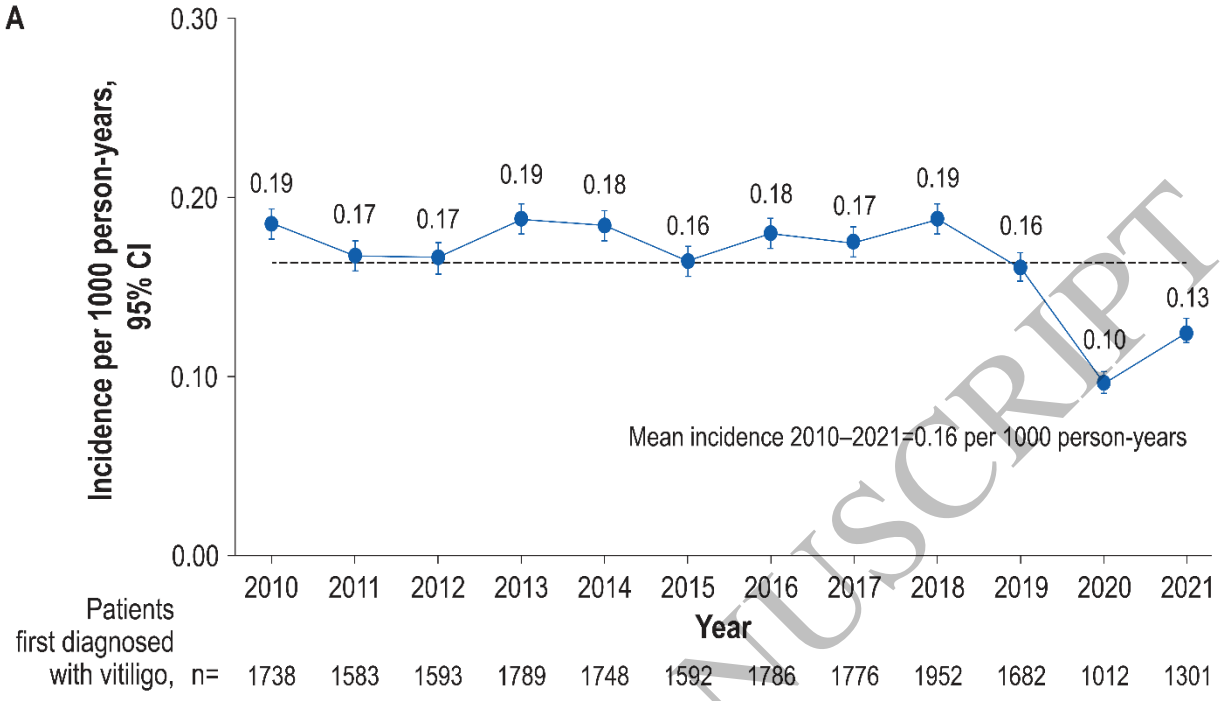

Figure 1A
165x93 mm (x DPI)

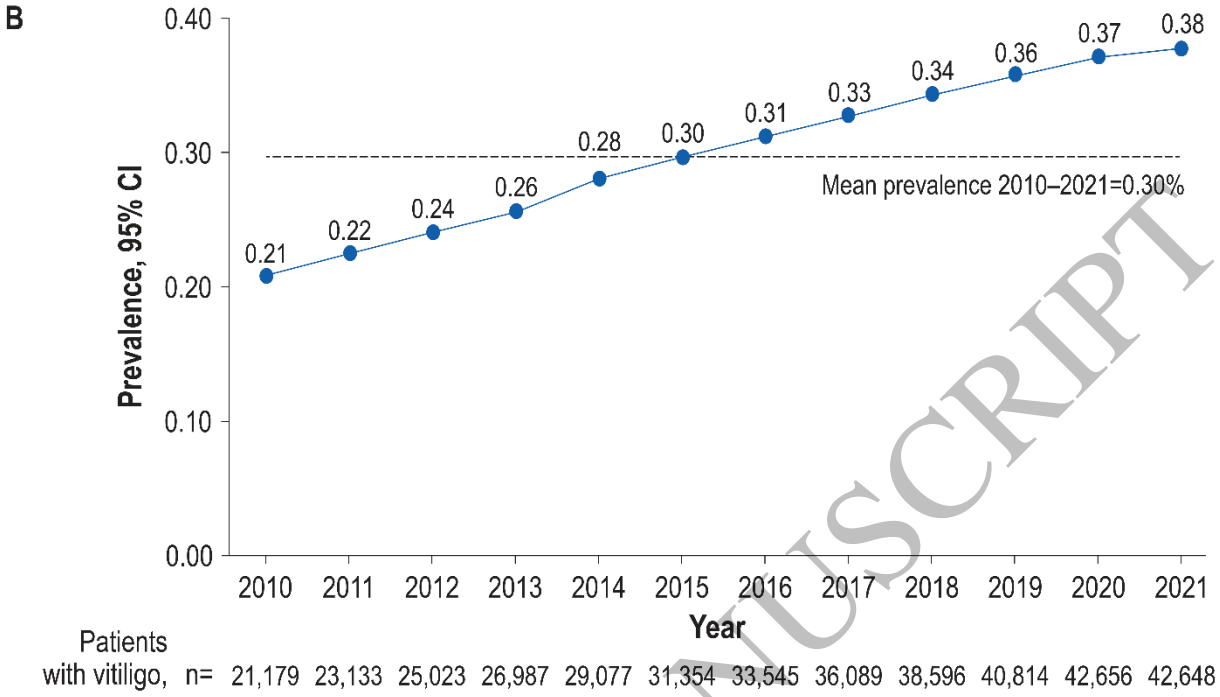

Figure 1B
165x93 mm (x DPI)

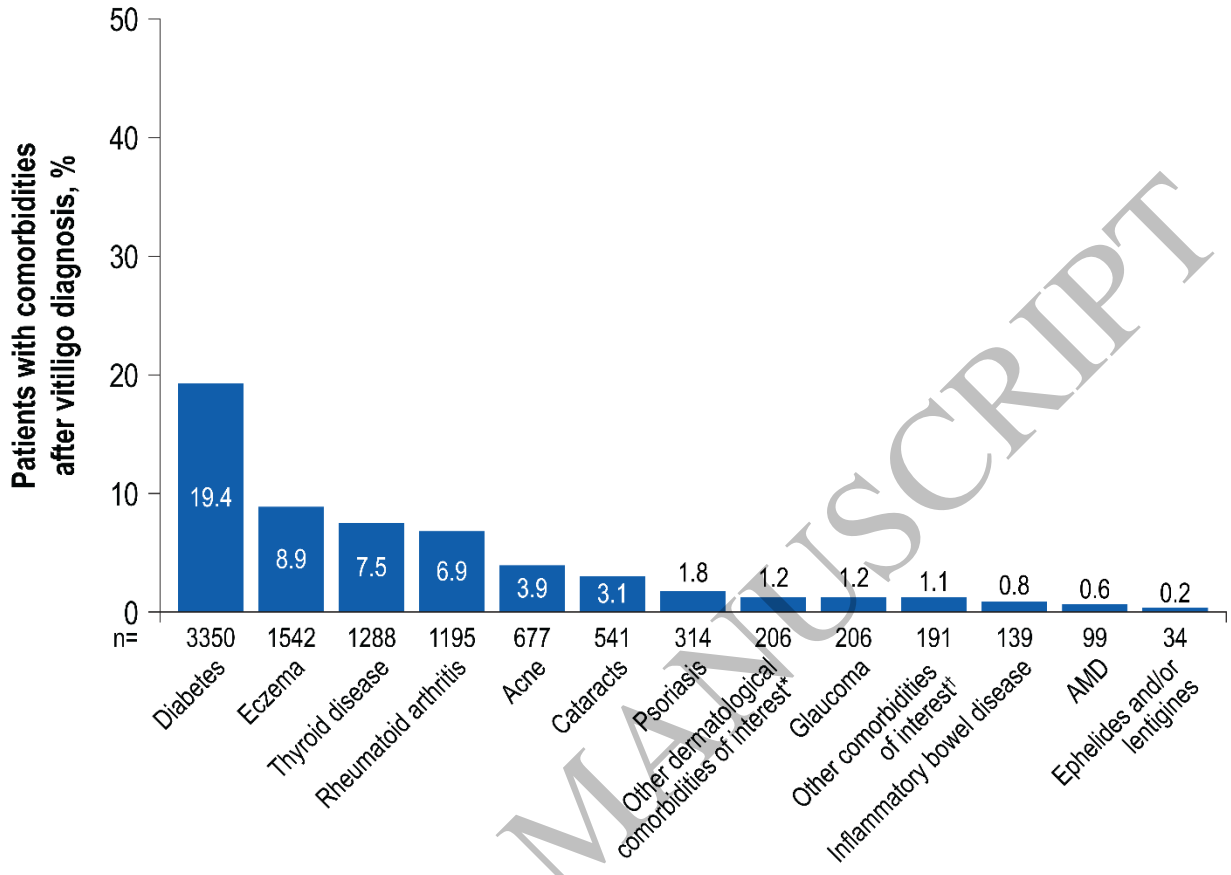

Figure 2

165x116 mm (x DPI)

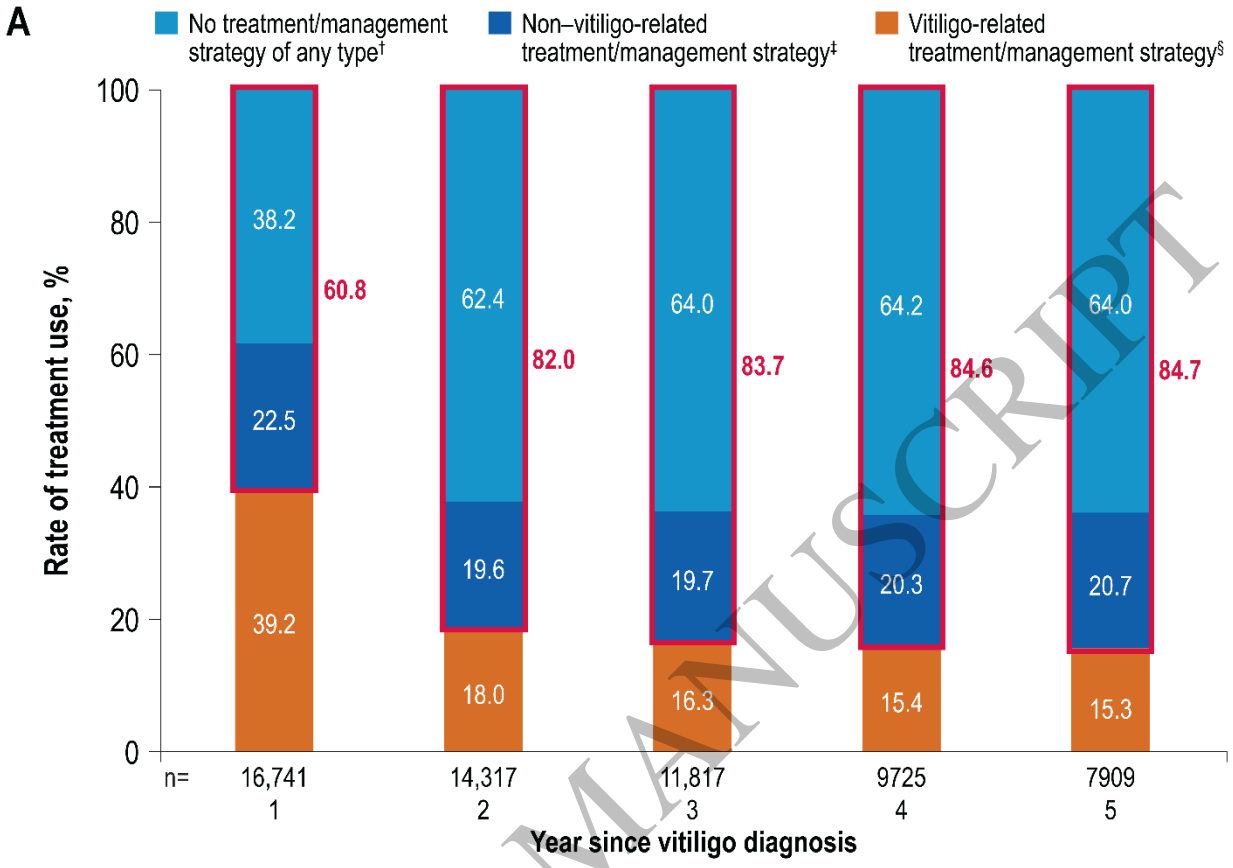

Figure 3A
165x114 mm (x DPI)

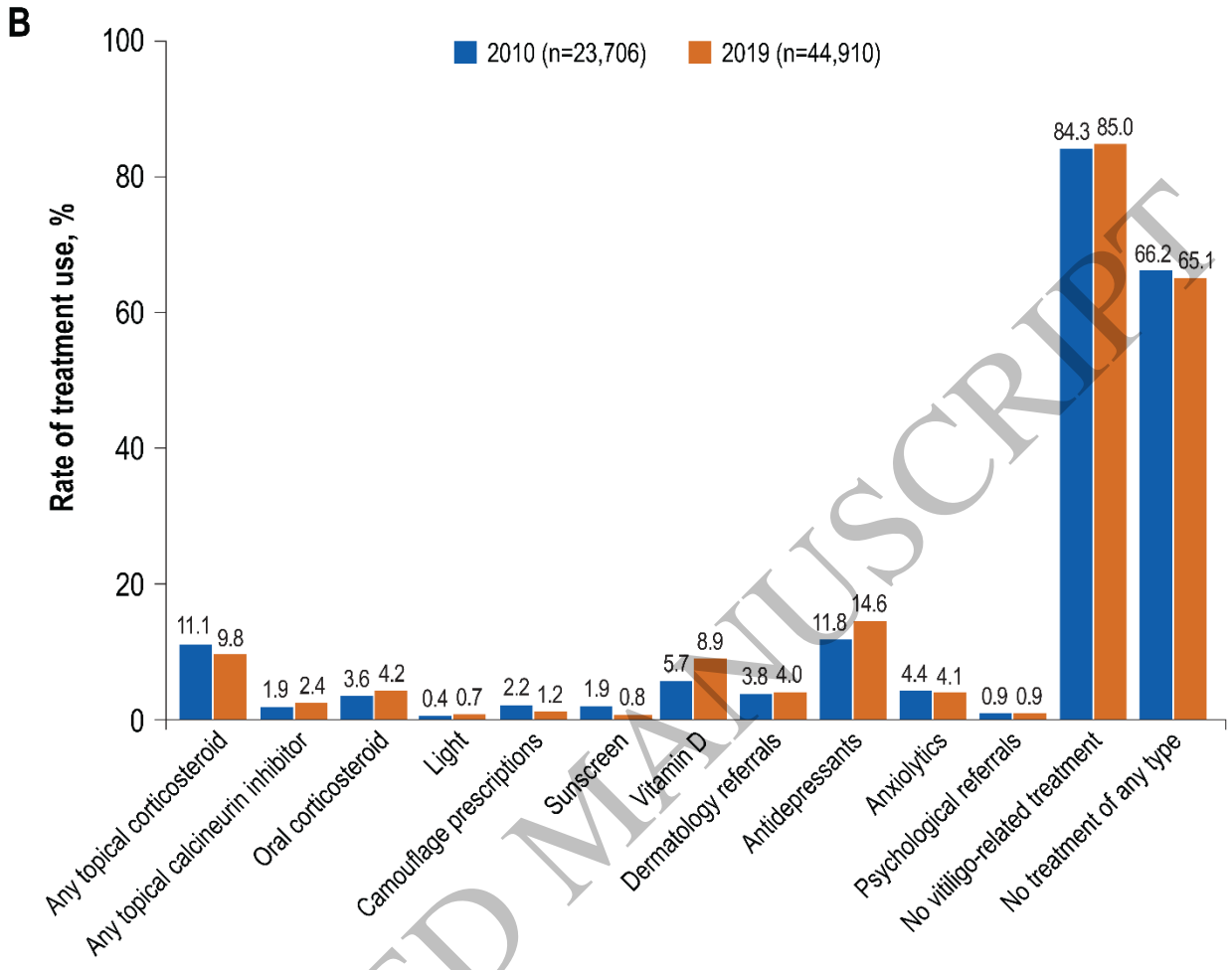

Figure 3B
165x129 mm (x DPI)

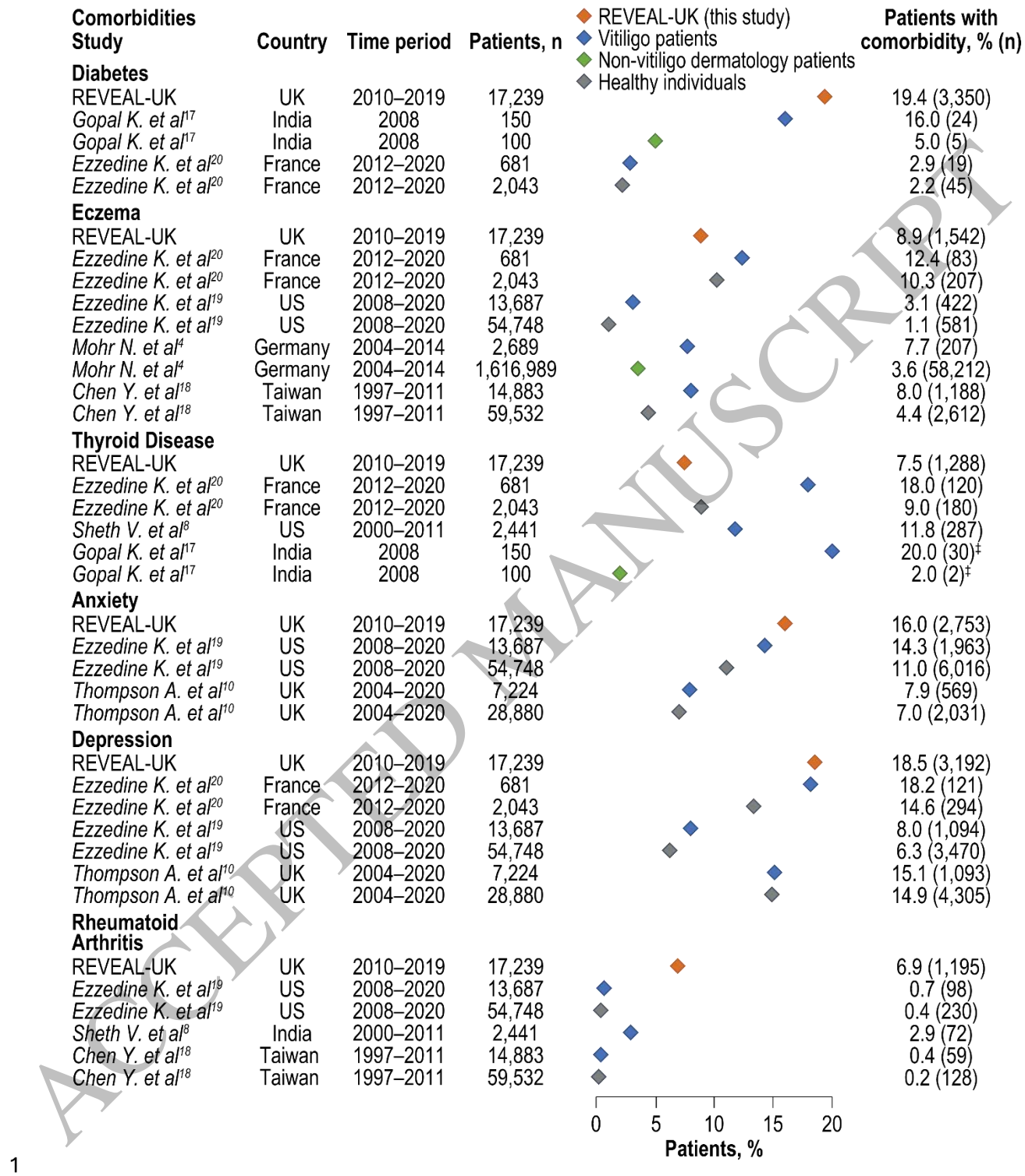

Figure 4

165x199 mm (x DPI)